Amendments to the Specification:

Please amend the specification to read as follows wherein strikeout in brackets [~~00~~] indicates deleted terminology and underlining, 00 indicates added terminology.

Please add the following new paragraph beginning on page 1, line 5:

This application is a continuation claiming priority to application Serial No. 09/877,804, filed June 7, 2001, which is a continuation of application Serial No. 08/207,814, filed March 7, 1994, now U.S. Patent No. 6,261,800 issued July 17, 2001, which is a continuation of application Serial No. 07/781,153, filed October 31, 1991 (now abandoned), which was filed under 35 U.S.C. § 371 from PCT/US90/02488, filed May 4, 1990, which is a continuation-in-part of application Serial No. 07/347,683, filed May 5, 1989 (now abandoned), the entire disclosures of which are hereby incorporated by reference.

Please replace the paragraph on page 4, line 34, with the following amended paragraph:

Figure 1 shows the cDNA (SEQ ID NO:1) and predicted amino acid sequence (SEQ ID NO:2) of the rat ovarian LH/CG-R. In the figure, chemically determined peptide sequences are indicated by bars atop corresponding sequences, with residues differing from those predicted indicated by white bars. Amino acid numbering begins at the N-terminal sequence found for the mature intact receptor (SEQ ID NO:3), with negative numbers for the encoded signal sequence. Putative extracel-lular N-linked glycosylation sites are marked by inverted triangles, and the proposed membrane-spanning hydrophobic sequences are enclosed in boxes. Overlined residues show location of similarity to soybean lectin (L.O. Vodkin et al., Cell 34:1023 (1983); D.J. Schnell et al., J. Biol. Chem. 262:7220 (1987) (Diflorus)).

Please replace the paragraph on page 5, line35, with the following amended paragraph:

Figure 6a and 6b show the cDNA (SEQ ID NO:5) and predicted amino acid sequence (SEQ ID NO:6) of rat testicular FSH-R. Amino acid numbering begins at the N-terminal sequence for the predicted mature receptor protein (SEQ ID NO:7), with negative numbers denoting the signal sequence.

Please replace the paragraph on page 42, line 32, with the following amended paragraph:

TABLE 2

ks: AAGGAGCTG(AG)TGGC(AG)C(C)GGAAGCCTGAGCCCA-ATGACTTC
(TC) (TC) (A)
GCCCCTGATGGTGCCCT (SEQ ID NO:9)

rsrc: TGCACCTCCTCGAAGCAGTTGCCATACAGCTTCAG-GGTCACA(CT)CTC (SEQ ID NO:10)
(GA)

fsrc: ACG(GG)GTCCAGGATG(CT)TGTGGCACCCTGGAAGGC(T)CC (SEQ ID NO:11)
(AT) (GA) (C)

Please replace the paragraph on page 43, line23, with the following amended paragraph:

The nucleotide (SEQ ID NO:1) and predicted amino acid sequence (SEQ ID NO:2) of the rat LH/CG-R cDNA with 43 nucleotides of 5' flanking and 759 nucleotides of 3' flanking sequence are shown in Figure 1. The translation initia-tion codon at position 1 defines the start of a 2100 nucleotide long open reading frame which encodes all independently determined peptide sequences. The predicted N-terminal amino acid sequence constitutes a signal peptide of 26 residues (G. von Heijne, Nucleic Acids Res. 14:4683 (1986)). The sequence following the signal peptide corres-ponds to the peptide determined from the uncleaved LH/CG-R (SEQ ID NO:3) poly-peptide. Hence, the mature LH/CG-R was concluded to begin with Arg and to be composed of 674 amino acid residues (Mr≈ 75 kDa).

Please replace the paragraph on page 44, line 23, with the following amended paragraph:

From these data, we postulate that the LH/CG receptor consists of a large N-terminal extracellular domain (SEQ ID NO:4) attached to a region that traverses the plasma membrane seven times, terminating with a small C-terminal cytoplasmic tail.

Please replace the paragraph on page 44, line 26, with the following amended paragraph:

It is likely that the extracellular domain (SEQ ID NO:4) is involved in binding the large glycoprotein hormones CG and LH. This assignment is consistent with biochemical data showing that a 64kDa water-soluble fragment of the LH/CG receptor can bind CG (Keinanen, K.P., Biochem. J. 239:83 (1986)) and with data from collagenase-treated cells.

Please replace the paragraph on page 44, line 30, with the following amended paragraph:

The extracellular region (SEQ ID NO:4) of the receptor has many notable features. Firstly, there are six potential sites for N-terminal glycosylation. Preliminary data suggests that most of these sites are likely to be glycosylated. Secondly, there is a site consisting of 10 amino acids which is identical to a region in the soybean lectin (Schnell, K.J. et al., J. Biol. Chem. 262:7220 (1987)). It is well known that although the degly-cosy-lated forms of CG and LH bind to the LH/CG receptor, they elicit little or no biological activity. Therefore, it will be interesting to test whether this site on the LH/CG receptor is involved in recognition of the carbohydrate chains of the hormone.

Please replace the paragraph on page 44, line 37, with the following amended paragraph:

Thirdly, the extracellular domain (SEQ ID NO:4) can be aligned into a 14-fold imperfectly repeated motif of approximately 25 amino acids. The composition of this leucine-rich motif is common to a number of other proteins. These include proteins of such widely diverse (or unknown) functions as the yeast adenylate cyclase (Kataoka, T. et al., Cell 43:493-505 (1985)), the Toll developmental gene of Drosophila (Hashimoto, C. et al., Cell 52:269 (1988)), the human serum alpha2 glycoprotein (Takahashi, N. et al., Proc. Natl. Acad. Sci. (U.S.A.) 83:1906 (1985)), the platelet 1b receptor for von Willebrand factor and thrombin (Lopez, J.A. et al., Proc. Natl. Acad. Sci. (U.S.A.) 84:5615 (1987)), and the extracellular matrix proteoglycan PG40 (Krusius, T. et al., Proc. Natl. Acad. Sci. (U.S.A.) 83:7683 (1986)). It should be pointed out that of these pro-teins, only PG40 appears to share an overall amino acid homology with the extracellular region of the LH/CG receptor. The biological significance of this leucine-rich repeat structure is not really known. It has been suggested that it may be able to form an amphipathic helical structure and, therefore, may be involved in interacting with both an aqueous environment and the plasma membrane. This suggests that upon binding CG or LH the extracellular domain of the LH/CG receptor may interact with the membrane-spanning regions of the receptor.

Please replace the paragraph on page 48, line 24, with the following amended paragraph:

The N-terminal half of the polypeptide chain (residues 1-341) (SEQ ID NO:4) presumably constitutes the extracellular domain (Fig. 1). Consonant with the glycoprotein nature of the LH/CG-R, there are six potential N-linked glycosylation sites within this domain. Preliminary evidence suggests that most of these sites are indeed glycosylated and this may account for the difference in molecular weight between the natural LH/CG-R (Mr $\approx$ 93 kDa) and the predicted mature unglycosylated poly-peptide (Mr * 75 kDa). In fact, molecular weights of CNBr fragments estimated by gel electrophoresis are consistent with an average contribution of 5-6 kDa per glycosylation site by oligosaccharide side chains.

Please replace the paragraph on page 53, line 35, with the following amended paragraph:

Polyadenylated RNA isolated from rat testicular Sertoli cells was used as a template for reverse transcriptase. The resulting cDNA served for the construction of a library in lgt10. An aliquot (1x106 clones) was screened for clones with sequence similarity to two probes derived from the LH/CG-R cDNA (nucleotides 1-483 and 1499-2604). Several positive clones were isolated and cloned cDNAs sequenced as described in F. Sanger et al., Proc. Natl. Acad. Sci. USA, 74:5463-5467 (1977) after subcloning into M13 vectors (J. Vieira and J. Messing, Meth Enzymol., 153:3-11 (1987)). The nucleotide (SEQ ID NO:5) and predicted amino acid (SEQ ID NO:6) sequences of this receptor are shown in Figure 6.

Please replace the paragraph on page 54, line 4, with the following amended paragraph:

The translation initiation codon at position 1 defines the start of a 2076 nucleotide open reading frame specifying an N-terminal 17 residue signal sequence followed by a largely hydrophilic domain of 348 residues of putatively extracellular location (SEQ ID NO:8). This domain contains three N-linked glycosylation sites. It is followed by a structure of 264 residues which comprises seven transmembrane segments. These segments are the hallmark of G protein-coupled receptors. Similar to other such receptors, the 63 residue C-terminus of the FSH-R is proposed to be located intracellularly and contains several amino acids (Ser, Thr, Tyr) whose phosphorylation may regulate receptor activity (K. Palczewski et al., Biochemistry, 27:2306-2313 (1988); J.L. Benovic et al., Proc. Natl. Acad. Sci. USA, 83:2797-2801 (1986)). However, these residues are not part of consensus phosphorylation sites as in other receptors. The mature FSH-R (SEQ ID NO:7) is predicted to comprise 675 amino acids (75K mol. wt.) and to constitute an integral membrane glycoprotein.